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(54) SUSTAINED RELEASE OF BIOLOGICALLY ACTIVE ORGANIC COMPOUNDS

(71) We, LAPORTE INDUSTRIES LIMITED, a British Company, of Hanover House, 14 Hanover Square, London, W.1, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to sustained release of biologically active organic compounds, that is, organic compounds having utility by virtue of their biological activity.

Examples of biologically active organic compounds are for example, insecticides, fungicides, molluscicides, herbicides, acaricides, nematocides or plant growth regulants. Such compounds usually take effect on being absorbed in the form of a solution in water into a target organism. It may be desirable to maintain the presence of one or more biologically active compounds in absorbable form over an extended period of time for example, for protection of growing crops from attack by diseases and pests. This may be accomplished by utilising sustained release compositions containing a biologically active compound which may be released slowly as a result of the effect of environmental conditions such as the effect of temperature, or moisture on the composition.

Sustained release compositions are subject to exacting performance requirements. There is, generally, a fairly narrow acceptable range of release rates, below which there is an insufficient concentration of the biologically active compound in absorbable form and above which there is an unacceptable degree of wastage. Preferably, therefore, the active compound is released from the sustained release composition at as uniform a rate as possible and at a rate which produces a level of concentration of active compound as close as possible to the optimum.

The present invention provides a sustained release composition comprising an inorganic particulate substrate having a cation exchange capacity, cations ionically bonded to the substrate, the cations having the formula

$$R_n X H_m^+$$

where x represents a nitrogen, phosphorus, antimony or arsenic atom having a valency of 4 or an oxygen, selenium, sulphur or tin atom having a valency of 3, R_n represents one or more organic radicals at least one of which contains a carbon-carbon chain of at least 10 carbon atoms and H_m represents sufficient hydrogen atoms, if any, required to satisfy the valency of X and a biologically active organic compound deposited onto the substrate.

Suitably the substrate has a structure based on silicon or phosphorus atoms and very suitably has a structure based on linked SiO_4 tetrahedra. Preferably the substrate comprises an anionic lattice comprising layers of linked SiO_4 tetrahedra possibly interleaved by layers of other minerals such as $Mg(OH)_2$ or $Al(OH_3)$, for example, a clay mineral. Suitable clay minerals may belong to any of the groups of minerals described in Kirk-Othmar, Encyclopaedia of Chemical Technology 2nd Edition, Volume 5, pages 541—557. Preferably the substrate is a member of the smectite group. Smectite clay minerals have structures based on that of the mineral

pyrophillite, which consists of superimposed layers each of which contains a plane of Al^{3+} ions sandwiched between two inward pointing sheets of linked SiO_4 tetrahedra. The central Al^{3+} section may be regarded as a layer of gibbsite, $Al_2(OH)_6$, in which 2 out of 3 OH ions are replaced by apical oxygens of an Si_4O_{10} pseudo-hexagonal network. The charge balance is upset by substitution in both octahedral (Al) and tetrahedral (Si) sites and is redressed by inter-layer cations, usually sodium or calcium cations. A typical extent of such substitution requires about 0.66 additional monovalent cations per formula unit and these ions are in general exchangeable. The smectite group includes the following groups of minerals:

Montmorillonite	$Si_8Al_{3.34}Mg_{0.66}(\frac{1}{2}Ca,Na)_{0.66}$
Beidellite	$Si_{7.34}Al_{0.66}Al_4(\frac{1}{2}Ca,Na)_{0.66}$
Nontronite	$Si_{7.34}Al_{0.66}Fe_4^{3+}(\frac{1}{2}Ca,Na)_{0.66}$
Saponite	$Si_{7.34}Al_{0.66}Mg_6(\frac{1}{2}Ca,Na)_{0.66}$
Hectorite	$Si_8Mg_{5.34}Li_{0.66}(\frac{1}{2}Ca,Na)_{0.66}$
Sauconite	$Si_{6.7}Al_{1.3}Zn_{4-5}(MgAl, Fe^{3+})_{2-1}(\frac{1}{2}Ca,Na)_{0.66}$

Many of the montmorillonite minerals have a high cation exchange capacity and are particularly suitable for use in the present invention. The majority of the exchangeable cations of the mineral are preferably sodium cations. A particularly suitable clay mineral which is, in its natural state, substantially in the sodium form, is Wyoming bentonite. Alternatively a synthetic clay mineral such as that produced by a process described in British Patent No. 1054111 or British Patent No. 1213122 may be used. Alternatively the exchangeable cations of the substrate may be alkaline earth metal cations.

Preferably the cation exchange capacity of the substrate is at least 0.5 m.eq/g and, particularly, at least 0.65 m.eq/g. Many smectite clay minerals and especially, many montmorillonite clay minerals have cation exchange capacities fulfilling this preference.

The cations utilised in the invention are known as 'onium' cations. In such cations the element X has its highest possible valency. This may be achieved by protonation, very suitably under acid conditions, of the compound RXH_m where H_m represents sufficient hydrogen atoms, minus 1, to satisfy the highest possible valency of X. Particularly suitable onium cations are based on nitrogen e.g. those prepared by protonating the corresponding amine, or quaternary ammonium compounds. In the onium cations utilised in this invention R_n in the general formula preferably contains from 10 to 30 carbon atoms. Examples of particularly suitable organic radicals having chains of average length of about 10 to 20 carbon atoms are those derived from tallow, soya or coco oil. Nitrogen based onium cations in the form of amines bearing such radicals are available under the Trade Name Duomeen. Preferably the onium cation is based on nitrogen and contains 2 3, or 4 organic radicals R, 1 or 2 of which contain a carbon-carbon chain of at least 10 carbon atoms and particularly preferably not more than 20 carbon atoms.

The cation exchange capacity of the substrate is preferably saturated with the onium cations. To attain this the onium cation is preferably in excess over the cation exchange capacity of the substrate. A suitable quantity of onium cation is above 1.0 and up to 1.3 times the cation exchange capacity of the substrate. In the manufacture of any of the compositions of this invention the substrate is preferably treated in the form of a dispersion in water at a concentration of, for example, from 1 to 12% by weight with the onium cation. It is an important factor in achieving an efficient adduction that the substrate be in a highly dispersed state. The presence of shear assists dispersion and a suitable way of attaining this is by means of a high shear stirrer. Additionally a dispersion agent, such as tetrasodium pyrophosphate, may be included in the suspension. The quantity of dispersing agent may be suitably in the range of 0.1% to 5% and preferably from 1% to 4% by weight of the substrate. If any aggregates of substrate remain undispersed it may be desirable to remove such aggregates by, for example, centrifuging. The onium cation may be added to the suspension of the substrate or may itself be dispersed in water, at, for example, a concentration of from 1% to 6% by weight, and the two dispersions

mixed by slowly adding the suspension of the onium compound to the dispersion of the substrate. Preferably the dispersion of the substrate and the mixed dispersions are maintained under shear throughout, and for a sufficient time after the mixing has been completed to allow the cation exchange to go to completion. A suitable time is for up to 30 minutes after mixing has been completed. Preferably the temperature is maintained throughout at from 10°C to 90°C depending on the thermal stability of the onium cation.

The derivative resulting from the cation exchange may be filtered and washed free of inorganic cations from the substrate and anions associated with the onium cation. Again depending on the thermal stability of the onium cation it may be necessary to control the temperature of drying carefully to avoid decomposition of the onium cation.

The derivative resulting from the ion exchange of an onium cation onto an organic substrate and bearing a biologically active organic compound in intimate association with the onium cations is capable of giving a controlled rate of release of the biologically active organic compound.

The inorganic substrate is inherently hydrophilic. The presence of the onium cation gives, to an extent, an organophilic character to the substrate which may facilitate, to an extent, the formation of the intimate association between the substrate and the deposited active compound. It is possible also, by suitable selection of the onium cation, so to reduce the hydrophilic character of the substrate as to assist in reducing the exposure of the active compound carried on it to moisture thereby reducing the tendency for the active compound to dissolve at an undesirably high rate. These effects make it possible to tailor the rate of release of active compound by simply selecting an onium cation having an organic chain or chains of suitable configuration and chain length to give the desired balance of organophilic and hydrophilic properties.

We also find that the particle size of the substrate has a marked effect on the rate of release of active compound. This parameter is particularly easy to control in the case of inorganic substrates such as clay minerals which are commonly available commercially in specified particle sizes or, if not, are easily sieved to the desired size. If the onium cation/active compound combination selected has too high a rate of release it may be possible to reduce that rate by using a substrate consisting of somewhat larger particles than might otherwise have been selected. The presence of very small particles may give rise to practical difficulties in distribution of the composition due to dusting but this may be alleviated by forming composite granules, or the like, containing an inert centre and bearing an outer coating comprising the composition of this invention and, if necessary, a suitable binder.

In one aspect of this invention the biologically active organic compound may be bound to the onium cation by a hydrolysable chemical linkage. In the presence of moisture the hydrolysable linkage tends to break and to release the active compound. This mechanism of release may have particular application where the biologically active compound is of a highly toxic nature since the formation of a chemical bond with one or more functional groups of the organic compound may reduce its toxicity and that of the sustained release composition during storage and handling operations. It is important to ensure that the hydrolysable linkage breaks in preference to the linkage between the onium cation and the inorganic substrate since otherwise the released active compound will still have the onium cation attached to it with a resulting effect on the solubility of the released active compound and also, probably on its activity. It is a very important feature of certain embodiments of this aspect of the invention that an ionic linkage between the siliceous inorganic substrate, and particularly a substrate comprising an anionic lattice comprising layers of linked SiO_4 tetrahedra, for example a clay mineral, and an onium cation can be particularly stable in the presence of water. As a result the onium cations tend to remain ion exchanged on the inorganic substrate under conditions which result in the breakage of the hydrolysable linkage but which might be expected, also, to result in at least the partial breakdown of an ionic linkage.

A hydrolysable linkage may be formed in a number of different reactions. The reaction of amines, or amides with carboxylic acids results in the formation of hydrolysable salts:—

$$R.COOH + H_2NR' \rightarrow RCOO^- \,{}^+H_3NR'$$

$$R.COOH + H_2NOCR' \rightarrow RCOO^- \cdot {}^+H_3NOCR'$$

$$R.COOH + Cl^- \, {}^+NH_3R \rightarrow RCOO^- \, {}^+H_3NR' + HCl$$

Additionally ester bonds are hydrolysable and are readily formed and may be employed in the practice of this invention.

Onium cations particularly suitable for use in the practice of this aspect of the invention are those having, after ion exchange to the substrate, free amine or ammonium groups capable of reacting with carboxylic acid groups on the biologically active compound, or free acid groups capable of reacting with amine or amide groups on the biologically active compound.

An example of a compound convertible to the onium form and having a carboxylic acid group is Armeen Z (Trade Mark), available from Armour Hess Chemicals Limited, which is produced by the reaction of primary coco amine and crotonic acid. An example of a compound convertible to the onium form and having an amine group is Duomeen (Trade Mark) which is also available from Armour Hess and is an assymmetrical diamine based on coco, tallow or soya residues. The coco, tallow or soya residues provides organophilic properties to a degree which makes these compounds suitable for use in the present invention.

It must be noted that while it is possible, according to one aspect of the invention, to utilise the presence of a hydrolysable chemical linkage between the biologically active compound and the onium cation to impart some degree of control over the rate of release, which possibility may be useful in some circumstances, there is in at least some instances a tendency for the rate of release to be slightly higher than if the biologically active compound is merely adsorbed, according to a further aspect of this invention, onto a substrate on which the onium cation has been ion exchanged without there being any or any substantial degree of hydrolysable chemical linkage therebetween. The major factor in achieving sustained release appears to be the presence and nature of the onium cation and the presence of an intimate association, achievable by deposition as hereafter described, between the biologically active compound and the onium cation.

Examples of biologically active compounds which may be utilised in this invention are listed in Table 1 which also identifies a functional group in each compound which could be utilised to form a hydrolysable linkage with a suitable onium cation and the particular biological activity associated with each compound coded as follows:—

H	—	Herbicide
F	—	Fungicide
N	—	Nematocide
I	—	Insecticide
PG	—	Plant Growth Regulant

TABLE 1

	Common Name	Chemical Name	Active as
contain amine groups	Aminotriazole	3-amino-1,2,4 triazole	H
	Asulam	4-aminobenzenesulphonyl carbamate	H
	Dicloran	2,6 dichloro-4-nitroaniline	F
	Menazon	S-4,6-diamino-1,3,5-triazin-2-ylmethyl OO-dimethyl phosphorodithioate	I
	Secbumeton	2-sec-butylamino-4-ethylamino-6-methoxy-1,3,5 triazine	H
	Terbutryne	2-tert-butylamino-4-ethylamino-6-methylthio-1,3,5-triazine	H
Contain carboxylic acid groups	Chloramben	3-amino-2,5 dichlorobenzoic acid	H
	Dalapon	2,2-dichloropropionic acid	H
	2,4,5-T	2,4,5-trichlorophenoxyacetic acid	H
	Dichlorprop	2-(2,4-dichlorophenoxy)propionic acid	H
	Dicamba	3,6-dichloro-2-methoxybenzoic acid	H
	2,4-D	2,4-dichlorophenoxyacetic acid	H
	Endothal	7-oxabicyclo(2,2,1)heptane-2,3-dicarboxylic acid	H
	Clorfenac	2,3,6-trichlorophenylacetic acid	H
		Naphthalene acetic acid	P, G
Contain amide or substituted amide groups	Terbucarb	2,6-di-tert-butyl-p-tolylmethyl-carbamate	H
	Monocrotophos	dimethyl cis-1-methyl-2-methyl carbamoylvinyl phosphate	I
	Bufencarb	3-(1-methylbutyl)phenylmethyl-carbamate	I
	Carbaryl	1-naphthylmethylcarbamate	I
	Carbofuran	2,3-dihydro-2,2-dimethylbenzofuran-7-ylmethylcarbamate	I
	Dimethoate	O,O-dimethyl-S-methylcarbamoyl-methyl phosphorodithioate	I
	Diuron	3-(3,4-dichlorophenyl)-1,1-dimethylurea	H
	Methomyl	1-(methylthio)ethylideneamino methylcarbamate	I
	Aldicarb	2-methyl-2-(methylthio)propylide-amino methylcarbamate	I, N
		Naphthalene acetamide	P, G

Organometallic compounds, that is organic compounds in which a metal is directly joined to carbon, may also be used in the practice of this invention. Examples of suitable biologically active organometallic compounds are found amongst the organo tin compounds, for example triethyl, tripropyl or triphenyl tin compounds such as tributyl tin oxide, organomercurials such as phenyl mercury acetate the organolead compounds such as triphenyl or tributyl lead acetate or the organo arsenic compounds such as triphenyl arsine compounds.

Examples of other biologically active compounds which may be utilised according to this invention are listed in the "Pesticide Manual 1974", issued by the British Crop Protection Council.

The quantity of biologically active compound used may be selected with reference to that theoretically required to react with the onium cation if it is desired that substantially all of the biologically active compound be chemically linked to the onium cation. Alternatively, a larger quantity of biologically active compound may be used if it is immaterial whether some or none is to be chemically linked to the onium cation. However, a major consideration in selecting the quantity is the desired duration of sustained release for a particular application bearing in mind the release rate found to be given by a particular sustained release composition.

Suitably the biologically active compound may be used in a quantity of from 10 mg to 250 mg per gram of the substrate in the dry state, without inclusion of the onium cation.

An intimate association between the biologically active compound and the onium cations may be achieved by depositing the biologically active compound onto the substrate, e.g. from a liquid medium. This may be achieved by adding biologically active compound to the onium-exchanged substrate as a solution, which may be an aqueous solution, in the presence of a pH regulator, if required to assist in the formation of a chemical linkage, after which the substrate may be recovered by filtration and dried. If the biologically active compound is to be physically adsorbed on the substrate it is preferred to contact the substrate with a solution of the active compound in a volatile solvent which may be removed leaving the active compound deposited onto the substrate.

The compositions of the present invention are in solid particulate form. Since it is preferred that the substrate be finely divided the composition is preferably pelleted, granulated or formed by known means into particles of a size suitable for distribution onto an area to be treated. In order to further improve the release characteristics of the compositions of the invention it may be desired to coat them with a delay coating of, for example, rosin so as to reduce the solubility of the active compound for an initial period.

A biological entity, such as an insect, fungus, mollusc, plant, nematode or mite, may be treated with an organic compound having biological activity towards the entity by treating the habitat of the entity with water which has acquired a content of the organic compound as a result of contact with a composition according the invention containing the organic compound. In practice, this may be achieved by contacting the habitat with the composition, relying on water present as a result, for example, of rainfall to leach the active compound from the composition.

It may be desired to treat a surface which comes into contact with moisture, such as the portion of a ship hull above the waterline, with a surface coating containing a suitable toxin to prevent the growth of organisms. A sustained release composition according to the present invention may be applied to such a surface as a constituent of a surface coating medium which allows the moisture to contact the sustained release composition so as to dissolve the active compound.

Another application for the compositions of this invention is application in the vicinity of a desired plant the biologically active compound being a herbicide and the purpose being to protect the plant from competing growth of herbacieous plants. Suitably the desired plant is a tree sapling.

The invention will now be illustrated by means of the following Experiments (which do not utilise compounds having utility by virtue of their biological activity and are therefore not according to the invention) which illustrate the concept of sustained release embodied therein by utilising methyl orange the release of which may be monitored colourimetrically.

In each Experiment a cylinder of Perspex (Trade Mark) 70 mm in diameter and fitted with a closure in the lower end, the closure being fitted with a drain tube

having a tap, was positioned vertically and loaded successively with the following layers of material:

1. Chelford Medium Sand — 1 cm depth approx.
2. Glasswool — 1.5 cm depth approx.
3. Whatman No. 3 (Trade Mark) Filter Paper
4. Chelford Medium Sand — 10 cm approx.
5. Sustained release composition mixed with 50 ml Chelford Medium Sand.
6. Chelford Medium Sand — 1 cm depth approx.
7. Whatman No. 3 Filter Paper

The sustained release composition used in each Experiment was produced as follows:

EXPERIMENT 1

50 g of calcium montmorillonite granules available from Laporte Industries Limited as SYK 22/44 Granules (the figures refer to the British Standard sieve mesh size range of the granules which corresponds to a particle size; i.e. BSS; of from 355 to 760 microns) was mixed with 3 g of methyl orange pigment which had previously been dissolved in 250 g of distilled water. The resulting slurry without first removing excess moisture was dried in an oven. The oven dried granules were found to have a skin of dried methyl orange which was removed by passing the granules through a 22 BSS sieve. The final loading of methyl orange on the granules was 24.75 mg/g. No onium cation was included.

EXPERIMENT 2

The method used was the same as for Experiment 1 but using a sieve fraction of from 85 to 100 mesh BSS obtained by grinding and sieving the granules used in Experiment 1. This corresponds to a particle size range of from 150 to 180 microns. The final loading of methyl orange on the granules was 16.50 mg/g. No onium cation was included.

EXPERIMENT 3

22.75 g of sodium bentonite belonging to the montmorillonite group of minerals available under the Trade Mark Volclay and having a cation exchange capacity of 0.79 milliequivalents/g (me/g) and a particle size range of from 32—53 microns and being equivalent to a dried weight of volclay of 20.0 g was dispersed in 400 mls distilled water and the dispersion was heated to 80°C. 5.76 g of an unsymmetrical diamine based on tallow oil available under the Trade Mark Duomeen was dispersed in 16 mls of 1 N HCl (sufficient in theory to protonate one of the two amine groups of the Duomeen to give an onium cation) and 200 mls distilled water and the dispersion was heated to 80°C. The two dispersions were mixed and stirred for 15 minutes, to allow the Duomeen, preferentially protonated at the secondary amine group, to ion exchange with sodium ions on the Volclay. The resulting adduct was filtered and washed free of chloride ions. 2.5 g methyl orange was dissolved in 250 g distilled water and mixed with the adduct which was filtered to remove excess moisture and dried in an oven. The final loading of methyl orange on the Volclay was 58.9 mg/g. Since the free amine groups of the Duomeen were unprotonated, except to such extent as may occur naturally in an aqueous medium, it is thought that no chemical bond, or substantially none, was formed between the methyl orange and the onium cation.

EXPERIMENT 4

The method was the same as that used for Experiment 3 except that the Volclay had a particle size range of below 32 microns. The final loading of methyl orange was again 58.9 mg/g.

EXPERIMENT 5

The method used was the same as for Experiment 4 except that the Duomeen was replaced by 10.78 g of dimethyl dioctadecyl ammonium chloride (available under the Trade Mark Arquad 2HT) and no acid was used since the Arquad 2HT, being a quaternary ammonium compound, is already suitable for adduction onto the Volclay. The final loading of methyl orange on the Volclay was 56.4 mg/g. No chemical bond could have formed between the methyl orange and the alkyl chains of the onium cation.

EXPERIMENT 6

The method used was the same as for Experiment 3 except that 32 mls of 1N HCl wa used so as to protonate both amine groups of the Duomeen. The final loading of methyl orange on the Volclay was 147.69 mg/g. It is thought that a substantial proportion of the methyl orange would have been bonded to free protonated primary amine groups on the onium cation by salt formation with the —SO_3^- residues on the methyl orange.

EXPERIMENT 7

The method used was the same as for Experiment 6 except that the Volclay had a particle size range of below 32 microns. The final loading of methyl orange was again 147.69 mg/g. Again it is thought that a substantial proportion of the methyl orange would have been chemically bonded to the onium cation.

The dosage of methyl orange included in layer number 5 of the column in each of Experiments 1 to 5 was 2.31 mg and in each of Experiments 6 and 7 was 2.6 mg and the appropriate quantity of sustained release composition to attain this dosage of methyl orange was used.

In the course of the Experiments a series of aliquots of 400 ml of distilled water were added to each column and the outlet tube was choked by means of the tap to give a dropwise flow from the column at a rate of 400 ml over 12 hours. Samples of the eluant were examined colourimetrically and the quantity of methyl orange eluted with each aliquot of distilled water was determined. The results expressed as a cumulative % methyl orange remaining are summarised in Table 2 over a series of 12 aliquots identified in column 1.

TABLE 2

Experiment	Wt. % Remaining						
Aliquots	1	2	3	4	5	6	7
1	76.84	62.99	97.38	95.58	75.58	95.85	82.19
2	48.44	41.35	93.46	85.23	51.38	84.47	53.04
3	41.95	30.57	89.13	75.10	40.47	71.43	36.92
4	39.28	24.25	84.50	66.88	34.24	60.58	27.31
5	37.63	19.13	79.38	59.39	29.87	50.20	19.09
6	35.93	14.50	74.06	52.38	27.00	41.28	14.55
7	35.79	12.94	69.84	48.18	26.06	39.02	13.63
8	35.79	10.56	66.38	45.06	24.94	35.75	12.63
9	34.84	6.97	61.01	40.82	22.78	30.60	10.82
10	34.84	5.17	56.81	37.14	21.13	27.83	9.90
11	34.84	3.05	53.48	34.93	19.49	25.45	9.48
12	–	2.06	50.19	33.11	18.93	23.84	9.06
Remarks	No onium cation	No onium cation	Little or no chemical bonding	Little or no chemical bonding	No chemical bonding	Substantial Chemical Bonding	Substantial Chemical Bonding

The following Examples illustrate the invention. Examples 1 and 2 are according to the invention and Example 3 is not according to the invention but is for comparative purposes.

In each Example a leaching column 7 cm in diameter and loaded as described below was used.

Depth of Layers — listed from top of column

2.5 cm	0.7 diameter glass beads.
	Whatman No. 541 filter paper.
10 cm	Chelford Medium Grade Sand.
1.8 cm	Mixture of sustained release composition and sand.
10 cm	Chelford Medium Grade Sand.
	Whatman No. 541 Filter Paper.

The loading of sustained release composition was 0.24 g. In Examples 1 and 2 the sustained release composition consisted of Volclay, having a cation exchange capacity of approximately 0.8 me/g, which had been ion exchanged with 0.75 me/g of mono protonated Duomeen and which had thereafter been treated with sufficient acid to protonate the free amine group of the Duomeen and treated with 2,4-dichlorophenoxyacetic acid (2,4-D). The Volclay carried 12.27% of the 2,4-D by weight against a theoretical maximum of 11.5%. In Example 1 the clay mineral was 36—44 BSS mesh size (420—345 microns diameter). In Example 2 the clay mineral was 60—100 BSS mesh size (250—150 microns). Example 3 was a repetition of Example 2 except that no Duomeen was used and the clay mineral was not acid treated.

In the course of the Examples a 400 ml aliquot of distilled water was allowed to flow slowly through the column in the course of a day and this was repeated using a further aliquot of 400 ml distilled water on each of 3 subsequent days. Each of the four eluates was examined as follows. A 25 ml sample of the eluate was extracted twice with 10 ml CCl_4. The CCl_4 was evaporated to 0.1 ml on a steam bath and 5.0 ml of 0.15% w/v chromotropic acid in methanol was added. The sample was then evaporated to dryness and 5 ml of concentrated sulphuric acid was added. The sample was then heated at 130°—135°C for 20 minutes. The sample was then cooled and made up to 50 ml with distilled water. If 2,4-D is present the sample is then wine red. Each sample is examined colourimetrically using a Eel Absorptiometer — No. 606 filter — at 565 mm in an appropriate size cell to enable an estimate of the quantity of 2,4-D present in the sample and, thereby, in the entire eluate, to be made by reference to a calibration curve which showed near linearity over the range 0—25 ppm 2,4-D.

The results, expressed as a cumulative weight % of the 2,4-D originally present in the sustained release composition are shown in Table 2.

TABLE 2

Eluate No.	Example No. 1	2	3
1	17	35.5	33.5
2	51.5	76	96.5
3	62.5	83	97
4	69.5	86.5	97.5

WHAT WE CLAIM IS:—

1. A sustained release composition comprising an inorganic particulate substrate having a cation exchange capacity, cations ionically bonded to the substrate, the cations having the formula

$$R_n X H_m^+$$

where X represents a nitrogen, phosphorus, antimony or arsenic atom having a valency of 4 or an oxygen, selenium, sulphur or tin atom having a valency of 3, R_n represents one or more organic radicals at least one of which contains a carbon-carbon chain of at least 10 carbon atoms and H_m represents sufficient hydrogen atoms, if any, required to satisfy the valency of X, and a biologically active organic compound deposited onto the substrate.

2. A composition as claimed in claim 1 wherein the substrate is a clay mineral.

3. A composition as claimed in claim 2 wherein the substrate is a clay mineral of the smectite group.

4. A composition as claimed in claim 3 wherein the substrate is a clay mineral of the montmorillonite group.

5. A composition as claimed in any preceding claim wherein the substrate has a cation exchange capacity of at least 0.5 m.eq/g.

6. A composition as claimed in any preceding claim wherein, in the formula, X represents a nitrogen atom.

7. A composition as claimed in claim 6 wherein, in the formula, n is equal to 2, 3 or 4 and one or two of the organic radicals represented by R_n contains a carbon-carbon chain of at least 10 carbon atoms.

8. A composition as claimed in claim 7 wherein in the formula each organic radical R contains not more than 30 carbon atoms.

9. A composition as claimed in any preceding claim wherein the biologically active organic compound is bound to the cations by a hydrolysable chemical linkage.

10. A composition as claimed in any preceding claim wherein the cation exchange capacity of the substrate is saturated by the cations.

11. A composition as claimed in any preceding claim wherein the biologically active compound is an insecticide.

12. A compound as claimed in claim 11 wherein the insecticide is S-4,6-diamino-1,3,5-triazin-2-ylmethyl O,O-dimethyl phosphorodithioate.

13. A composition as claimed in claim 11 wherein the insecticide is dimethyl cis-1-methyl-2-methyl carbamoylvinyl phosphate.

14. A composition as claimed in claim 11 wherein the insecticide is 3-(1-methylbutyl) phenylmethylcarbamate.

15. A composition as claimed in claim 11 wherein the insecticide is 1-naphthyl-methylcarbamate.

16. A composition as claimed in claim 11 wherein the insecticide is 2,3-dihydro-2,2-dimethylbenzofuran-7-ylmethylcarbamate.

17. A composition as claimed in claim 11 wherein the insecticide is O,O-dimethyl-S-methylcarbamoylmethyl phosphorodithioate.

18. A composition as claimed in claim 11 wherein the insecticide is 1-(methylthio)ethylideneamino methylcarbamate.

19. A composition as claimed in claim 11 wherein the insecticide is 2-methyl-2-(methylthio) propylideamino methylcarbamate.

20. A composition as claimed in any one of claims 1 to 10 wherein the biologically active compound is a herbicide.

21. A composition as claimed in claim 20 wherein the herbicide is 3-amino-1,2,4 triazole.

22. A composition as claimed in claim 20 wherein the herbicide is 4-aminobenzenesulphonylcarbamate.

23. A composition as claimed in claim 20 wherein the herbicide is 2-sec-butylamino-4-ethylamino-6-methoxy-1,3,5 triazine.

24. A composition as claimed in claim 20 wherein the herbicide is 2-tert-butylamino-4-ethylamino-6-methylthio-1,3,5-triazine.

25. A composition as claimed in claim 20 wherein the herbicide is 3-amino-2,5 dichlorobenzoic acid.

26. A composition as claimed in claim 20 wherein the herbicide is 2,2-dichloropropionic acid.

27. A composition as claimed in claim 20 wherein the herbicide is 2,4,5-trichlorophenoxyacetic acid.

28. A composition as claimed in claim 20 wherein the herbicide is 2-(2,4-dichlorophenoxy) propionic acid.

29. A composition as claimed in claim 20 wherein the herbicide is 3,6-dichloro-2-methoxybenzoic acid.

30. A composition as claimed in claim 20 wherein the herbicide is 2,4-dichlorophenoxyacetic acid.

31. A composition as claimed in claim 20 wherein the herbicide is 7-oxabicyclo(2,2,1)heptane-2,3-dicarboxylic acid.

32. A composition as claimed in claim 20 wherein the herbicide is 2,3,6-trichlorphenylacetic acid.

33. A composition as claimed in claim 20 wherein the herbicide is 2,6-di-tert-butyl-p-tolymethyl-carbamate.

34. A composition as claimed in claim 20 wherein the herbicide is 3-(3,4-dichlorophenyl)-1,1,-dimethylurea.

35. A composition as claimed in any one of claims 1 to 10 wherein the biologically active compound is a fungicide.

36. A composition as claimed in claim 35 wherein the fungicide is 2,6 dichloro-4-nitroaniline.

37. A composition as claimed in any one of claims 1 to 10 wherein the biologically active compound is a nematocide.

38. A composition as claimed in claim 37 wherein the nematocide is 2-methyl-2-(methylthio)propylideamino methylcarbamate.

39. A composition as claimed in any one of claims 1 to 10 wherein the biologically active compound is a plant growth regulant.

40. A composition as claimed in claim 39 wherein the plant growth regulant is naphthalene acetic acid.

41. A composition as claimed in claim 39 wherein the plant growth regulant is naphthalene acetamide.

42. A composition as claimed in any one of claims 1 to 10 wherein the biologically active compound is an organometallic compound.

43. A composition as claimed in claim 42 wherein the biologically active compound is an organotin compound.

44. A composition as claimed in claim 43 wherein the biologically active compound is tributyl tin oxide.

45. A composition as claimed in any preceding claim wherein the biologically active compound is in the composition in from 10 to 250 mg per gram of substrate, the substrate being weighed when dry and without inclusion of the onium compound.

46. A composition as claimed in claim 1 and substantially as described herein.

47. A process for treating a biological entity with an organic compound having biological activity towards said entity comprising exposing the habitat of the biological entity to contact with water which has acquired a content of said organic compound as a result of contact with a composition as claimed in any preceding claim.

48. A process as claimed in claim 47 wherein the organic compound is a herbicide and the composition is applied to the vicinity of a plant towards which the herbicide has no activity to protect the said plant from competing growth.

49. A process as claimed in claim 48 wherein the plant to be protected is a tree sapling.

50. A process as claimed in claim 47 wherein the composition is included in a surface coating medium and wherein the medium is applied to a surface subject to contamination by the growth thereon of biological entities.

51. A process as claimed in claim 47 and substantially as described herein.

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